

## RACHEL'S ENVIRONMENT & HEALTH NEWS

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### A NEW WAY TO INHERIT ENVIRONMENTAL HARM

by Tim Montague\*

New research shows that the environment is more important to health than anyone had imagined. Recent information indicates that toxic effects on health can be inherited by children and grandchildren, even when there are no genetic mutations involved.[1] These inherited changes are caused by subtle chemical influences, and this new field of scientific inquiry is called "epigenetics." [2]

Since the 1940s, scientists have known that genes carry information from one generation to the next, and that genes gone haywire can cause cancer, diabetes, and other diseases. But scientists have also known that genes aren't the whole story because identical twins -- whose genes are identical -- can have very different medical histories. One identical twin can be perfectly healthy while the other develops schizophrenia or cancer -- so the environment must play a significant role, not merely genes.

What's surprising is that scientists are now revealing that these environmental effects can be passed from one generation to the next by a process called "epigenetics," with far-reaching implications for human health. Epigenetics is showing that environmental influences can be inherited -- even without any mutations in the genes themselves[1] -- and may continue to influence the onset of diseases like diabetes, obesity, mental illness and heart disease, from generation to generation.

In other words, the cancer you get today may have been caused by your grandmother's exposure to an industrial poison 50 years ago, even though your grandmother's genes were not changed by the exposure.[1] Or the mercury you're eating today in fish may not harm you directly, but may harm your grandchildren.

This emerging field of epigenetics is causing a revolution in the understanding of environmental influences on health. The field is only about 20 years old, but is becoming well-established. In 2004, the National Institutes of Health granted \$5 million to the Johns Hopkins Medical School in Baltimore to start the Center for Epigenetics of Common Human Disease.

The latest information appears in a new study by Michael Skinner and colleagues at the University of Washington, published in the June 3 issue of Science magazine. Skinner found that mother rats exposed to hormone-mimicking chemicals during pregnancy gave birth to four successive generations of male offspring with significantly reduced fertility.[3] Only the first generation of

mothers was exposed to a toxin, yet four generations later the toxic effect could still be detected.

Prior to this study, scientists had only been able to document epigenetic effects on the first generation of offspring. These new findings suggest that harm from toxins in the environment can be much longer lasting and pervasive than previously known because they can impact several generations.

And therefore a precautionary approach to toxics is even more important than previously believed. (See Rachel's 765, 770, 775, 781, 787, 789, 790, 791, 802, 803, 804.)

Over the past sixty years doctors and scientists have pieced together a picture of the genetic basis for life and some of the genetic causes of human and animal disease. Genes regulate the production of proteins – the essential building blocks of life. Genes are composed of a finite series of letters (a code made up of Cs, Ts, As, and Gs, each representing a nucleotide) embedded in long strands of DNA. DNA is the large molecule, composed of genes, that carries the genetic inheritance forward into the next generation.

There are approximately three billion 'letters' in the human genetic code. Science has long understood that when a gene mutates -- that is, when a typo is introduced -- it can have far-reaching effects for the cell, the tissue and the organism as a whole. For example, a genetic mutation caused by too much sun (ultraviolet radiation), could result in abnormal uncontrolled cell growth which could lead to skin cancer which could spread throughout your body. Stay in the shade and you reduce your risk.

But now scientists are seeing that disease can be passed from generation to generation without any genetic mutations.[1] The DNA molecule itself gets another molecule attached to it, which changes the behavior of the genes without changing the genes themselves.[1] The attachment of these additional molecules is caused by environmental influences -- but these influences can then be passed from one generation to the next, if they affect the germ cells, i.e., the sperm or the egg.

Scientists have, so far, discovered three different kinds of "epigenetic" changes that can affect the DNA molecule and thus cause inheritable changes. One is the methyl molecule.

Scientists began to see direct connections between human diseases like cancer and these subtle genetic variations like methylation in 1983 when Andrew Feinberg and his colleagues at Johns Hopkins found that cancer cells had unusually low incidence of DNA-methylation.[4] Methyl is a molecule of one carbon atom and three hydrogen atoms. Together they attach to a strand of DNA altering its three-dimensional structure and the behavior of specific genes in the DNA strand. It turns out that methylation works like a volume control for the activity of individual genes. Whereas genetic mutations are typos and relatively easy to test for, epigenetic changes are analogous to the formatting of the text (e.g. font, size, and color) and are much less-well understood.

Over the past 20 years, Feinberg and many other cancer specialists have documented the widespread influence of epigenetics on the development of cancer in humans and laboratory animals.

[5] So epigenetics is changing our traditional picture of common chemicals, like DDT. DDT is a powerful environmental toxin -- once it enters a living thing it mimics the behavior of natural hormones -- resulting in abnormal sexual and reproductive development. Widespread use of DDT in the 1940s and 1950s is associated with large scale declines in some bird populations (like the Peregrin falcon) because DDT causes birds' eggshells to thin, and thus the eggs crack before the embryo can develop into a chick.

When persistent environmental pollutants (like DDT) are phased out, we might be falsely lulled into believing that we have solved the problem. The thinking is logical -- remove the toxin from the environment and you get rid of the toxic effects. Not so according to the findings of Skinner and his colleagues.

The Skinner study tells us that phasing out dangerous toxins doesn't end the problem -- because the damage done by exposures decades ago could still flow from generation to generation via epigenetic pathways.

Skinner and his colleagues treated groups of pregnant rats, some with methoxychlor and some with vinclozolin. Methoxychlor is a replacement for DDT, a pesticide used on crops and livestock and in animal feed. Vinclozolin is a fungicide widely used in the wine industry. It is just one of a suite of widely used chemicals from flame-retardants to ingredients in plastics that can cause reproductive abnormalities in laboratory animals.

Both methoxychlor and vinclozolin are known hormone disruptors (see Rachel's 486, 487, 499, 501, and 547). Male offspring of these pesticide-treated mothers had reduced fertility (lower sperm count, reduced sperm quality), which was not a surprising finding. The scientists then bred these offspring, and again the male offspring had reduced fertility. This came as a complete surprise. Over 90% of the male offspring in four generations of the test animals had reduced fertility.

Skinner's report concludes that genetic mutations are highly unlikely to produce such a strong signal in the treated animals and that DNA-methylation is the likely mechanism responsible for the observed decline in male fertility.

Treating the mother rats during pregnancy apparently re-programmed the genetic material in the male offspring so that all subsequent male offspring suffered lower fertility from this environmental factor.

Skinner believes that his findings in rats could explain the dramatic rise in breast and prostate cancers in humans in recent decades (see Rachel's 346, 369, 375, 385 and 547) as partly due to the cumulative effects of multiple toxins over several generations.

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Of course all this new information makes the control of toxic chemicals even more important than previously thought. The health of future generations is at stake.

The development of epigenetics also greatly complicates toxicity testing, and chemical risk assessment. Epigenetics tells us that much additional toxicity testing will be needed. So far, there are no standardized, government-approved protocols for conducting epigenetic tests.

Until such protocols emerge (which could take years), and a great deal of expensive testing has been completed (requiring many more years), risk assessors will have to acknowledge that -- so far as epigenetics is concerned -- they are flying blind.

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